HEPATITIS A, HEPATITIS B, MEASLES, MUMPS, RUBELLA AND VARICELLA SEROPREVALENCE IN TURKISH ADOLESCENT NURSING STUDENTS

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ABSTRACT

Objective: *Healthcare workers and healthcare school students have increased risk of contracting and transmitting viral diseases such as hepatitis A, hepatitis B, measles, mumps, rubella, and varicella.*

This study aimed determining the seroprevalence of these infections in Turkish adolescent nursing students.

Material and Method: *Specific immunoglobulin G antibodies were studied by Enzyme-Linked Immunosorbent method in blood samples of students before the hospital internship; the data were collected retrospectively. A questionnaire was applied to 320 students participating in this cross-sectional study with 14 questions, prospectively.*

Results: *Study group was vaccinated against hepatitis B, measles, rubella, and mumps according to the routine vaccination schedule; 14 students had also received hepatitis A vaccine. Among 320 students [(70.9% girls, median 17 years (16-18)], the seroprevalence of hepatitis A, hepatitis B, measles, mumps, rubella and varicella were 17%, 93%, 82.2%, 98.7%, 98.6%, and 93%, respectively.*

Conclusion: *The majority of nursing students were susceptible to hepatitis A virus (83%) and measles virus seropositivity was low (82.2%) in this study. Because of this, we recommend that students be screened for vaccine-preventable viral diseases, especially hepatitis A and measles, at admission to school.*

Keywords: *Adolescent, immunization, infectious diseases, nursing students, prevention.* **Nobel Med 2019; 15(1): 33-40**

TÜRK ERGEN HEMŞİRELİK ÖĞRENCİLERİNDE HEPATİT A, HEPATİT B, KIZAMIK, KIZAMIKÇIK, KABAKULAK VE SUÇİÇEĞİ SEROPREVALANSI

ÖZET

Amaç: Sağlık çalışanları ve sağlık okulu öğrencileri, hepatit A, hepatit B, kızamık, kabakulak, kızamıkçık ve suçiçeği gibi viral hastalıklarla karşılaşma ve bulaştırma açısından artmış risk altındadır. Bu çalışmanın amacı, Türk ergen hemşirelik öğrencilerinde bu enfeksiyonların seroprevalansını saptamaktır.

Materyal ve Metot: Öğrencilerin hastane stajı öncesi kan örneklerinden Enzim-Linked Immunosorbent yöntemiyle spesifik immunoglobulin G antikorları çalışıldı; veriler geriye dönük olarak toplandı. Bu kesitsel çalışmaya katılan 320 öğrenciye ileriye dönük olarak 14 soruluk anket uygulandı.

Bulgular: Çalışma grubu rutin aşılama programına uygun olarak hepatit B, kızamık, kızamıkçık ve kabakulağa karşı aşılıydı; 14 öğrenci de hepatit A aşısı yaptırmıştı. Çalışmaya alınan 320 öğrencinin [(%70,9 kız, medyan 17 yıl (16-18)], hepatit A, hepatit B, kızamık, kabakulak, kızamıkçık ve suçiçeği seroprevalansı sırasıyla %17, 93%, %82,2, %93,7, %98,6 ve %93 bulundu.

Sonuç: Çalışmamızda hemşirelik öğrencilerinin önemli bir kısmının hepatit A'ya duyarlı (%83) ve kızamık virusüne karşı düşük seropozitiviteye (%82,2) sahip olduğu saptandı. Bu nedenle, öğrencilerin okula kabulünde, aşı ile korunulabilir viral hastalıklara özellikle de hepatit A ve kızamığa karşı tarama yapılmasını önermekteyiz.

Anahtar kelimeler: Ergen, bağışıklama, enfeksiyon hastalıkları, hemşirelik öğrencisi, korunma. **Nobel Med 2019; 15(1): 33-40**

INTRODUCTION

Healthcare workers (HCWs) and healthcare school students are at risk for exposure to serious, and sometimes deadly, diseases. Healthcare personnel that work directly with patients or handle material that could spread infection, should get appropriate vaccines to reduce the chance that they will get or spread vaccine-preventable diseases.[1] On the basis of documented nosocomial transmission, HCWs and healthcare school students are considered to be at significant risk for acquiring or transmitting hepatitis B, influenza, measles, mumps, rubella, and varicella; all of these diseases are vaccine-preventable. All healthcare personnel should protect themselves and susceptible patients by receiving appropriate immunizations. High immunization rates and sustaining immunization levels are necessary in these groups, because of the reasons mentioned above.[2]

There are several reports of outbreaks of measles, rubella, and varicella zoster epidemics, which develop at healthcare workers.[3-7] Because of these reasons, infection screening and evaluation of immunity status during registration are recommended.[1,2,8]

Nursing students (NS) in Turkey begin their hospital practice in adolescent age and therefore the risk of exposure to various infectious agents and vaccine preventable viral infections is higher than the other adolescent population. The students are very young and inexperienced during their hospital practice trainings and are exposed to many infectious diseases.

Although there are studies evaluating immunization status and carrier frequency against infectious diseases in health college and medical faculty students, there is only one study carried out among the NS on this subject, in Turkey.[9] Çetinkol and Yıldırım evaluated the seroprevalence of hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (anti-HCV), hepatitis B surface antibody (anti-HBs), and hepatitis A antibody (anti-HAV IgG).[9] However, authors had not investigated the seropositivity of measles, mumps, rubella, and varicella among NS.

The aim of this study is to determine the immune status of the NS against hepatitis A, hepatitis B, measles, mumps, rubella and varicella, who study at the nursing schools, in Ankara, Turkey. This study can contribute to the development of vaccine program changes required for appropriate immunization during school registration and before the beginning of the hospital practice.

MATERIAL AND METHOD

Nursing students who were directed to hospital for internship were enrolled in the study. The nursing students had to give blood test [HBsAg, anti-HCV, anti-HBs, anti-HAV IgG, anti-measles immunoglobulin G (anti-measles IgG), anti-mumps immunoglobulin G (anti-mumps IgG), anti-rubella immunoglobulin G (anti-rubella IgG), anti-varicella zoster virus immunoglobulin G (anti- VZV IgG), and human immunodeficiency virus antibody (anti-HIV)] that is required as a procedure of during internship

application to our hospital. In this study, the analyses of these tests were evaluated, retrospectively, and a questionnaire was given to the same students, prospectively. This study was performed between September 2014 and September 2015.

This study was reviewed and approved by the Ankara Training and Research Hospital's "Research Ethics Committee" (No: 5272).

Before being included in the study, they were asked whether they agreed to participate in the study; all the cases agreed to participate in the study. A signed written informed consent was obtained from the adolescents and their parents. Exclusion criteria in this study were the history of using immunosuppressive treatment (including steroids) (n=2) or the history of blood and/or blood product transfusion (n=7); according to this, a total of nine students were left out of the study.

The students were required to fill a questionnaire that was prepared by the authors for collecting their demographic data (Appendix). The data from the Turkish Labor Union Confederation was used to determine the income status of the families.[10] Moreover, the students were questioned if they had appropriate vaccines for the Ministry of Health Vaccination Schedule, and if they had an additional vaccine which is not included in the Ministry of Health Vaccination Schedule. They also reported their last vaccination time.

All of the NS had been vaccinated according to the Ministry of Health 1997-1999 Vaccination Schedule.[11,12] There were 14 students who had hepatitis A vaccine (two doses) not found in the Ministry of Health 1997-1999 Vaccination Schedule.

Hepatitis B vaccine was added to the Ministry of Health Vaccination Schedule in 1998. It was applied as three doses during infancy and one rapel at the primary school to the children who were born in 1998 and after. It had been applied as three doses during primary school to the children who were born in 1997.[11,12] Because of this fact, the study group was divided into two groups; one for the children born in 1997, and one for the children born in and after 1998 for the evaluation of the anti-HBs levels.

Measles vaccines had been applied to all students in the study group, when they were nine months old, and a second dose at the first grade; additionally they had an extra dose in the “measles vaccine day”. The fourth dose had been vaccinated with measles, mumps, rubella (MMR) vaccine at the primary school.[11,12]

Five-milliliter blood samples were taken from the NS and centrifuged at 3000 rpm. After separating serum, antibodies to the hepatitis B core antigen (anti-HBc), HBsAg, anti-HBs, anti-HCV, anti-HAV IgG, anti-measles IgG, anti-mumps IgG, anti-rubella IgG, anti- VZV IgG, anti-HIV titrations were studied.

Hepatitis B surface antigen, anti-HBs, anti-HBc, anti-HCV, and anti-HIV titrations were examined by Enzyme Linked Immunosorbent Assay (ELISA) method (Abbott axsym). An anti-HBs level ≥10 mIU/mL was accepted as seropositive. Hepatitis A antibody was investigated by chemiluminescence micro particle enzyme immunologically test method (Abbott, Architect, Germany). Measles, rubella, mumps and varicella zoster virus (VZV) antibodies were studied by using micro ELISA (RADIM®, Italy) kits, in a completely automated system (Alisei Quality System, SEAC, Italy), as the company suggested. All the results were evaluated according to the directions from the manufacturing company. All NS tested seronegative for any vaccine preventable disease were referred for vaccination. Due to the technical problems, it was not possible to perform all of the tests to NS, because of the completion of the test kits intermittently in the Hospital.

The data was transferred to computer by using statistical analysis software package program (SPSS 15.0). It was examined by Kolmogorov Smirnov test, whether the distribution of continuous and discrete numeric variables were close to normal.

Descriptive statistics were shown in the median form for the continuous and discrete variables, and in the percentage form for the categorical variables. The importance of the difference in terms of median values between the groups was researched using the Mann Whitney U test. Categorical variables were evaluated using the Chi-Square test. Statistical significance for all analyses was set at a p value < 0.05.

RESULTS

Study subjects were adolescents with a median age of 17 years (range: 16-18 years) (Table 1). Of the 320 NS who participated in the study, 227 (70.9%) were females.

Fifty-eight (18.1%) of the adolescents had an extra vaccine which was not included in the Ministry of Health Vaccination Schedule. These were influenza (n=38), hepatitis A (n=13), hepatitis B (n=4), tetanus (n=2), varicella (n=1) and influenza+ hepatitis A (n=1).

Table 1. Sociodemographic characteristics of adolescents attending to nursing students*

Sociodemographic Characteristics	n=320
Age (years), median (min-max)	17 (16-18)
Premature born, n (%)	13 (4.1)
Education level of the mother, n (%)	
Illiterate	8 (2.5)
Literate	7 (2.2)
Primary school	128 (40.0)
Secondary school	88 (27.5)
High school/ University graduate	89 (27.8)
Education level of the father, n (%)	
Illiterate	1 (0.3)
Literate	1 (0.3)
Primary school	64 (20.0)
Secondary school	88 (27.5)
High school/ University graduate	166 (51.9)
Income status of the family, n (%)	
Under the minimum wage	4 (1.3)
Gets minimum wage	32 (10.0)
Income is more than minimum wage	284 (88.7)
Cigarette smoking, n (%) **	
None	132 (41.3)
Father	161 (50.3)
Mother	83 (26.0)
Student	18 (5.7)
The chronic disease of the student, n (%)	21 (6.6)
Asthma	4 (19.0)
Raynaud phenomenon	4 (19.0)
Rheumatic disease	3 (14.3)
Familial Mediterranean fever	3 (14.3)
Allergic rhinitis	2 (9.4)
Migraine	1 (4.8)
Cardiac disease	1 (4.8)
Diabetes mellitus	1 (4.8)
Hypothyroidism	1 (4.8)
Anemia	1 (4.8)

*: Column percent, **: More than one sign

All of the NS tested seronegative for HBsAg, anti-HBc IgM, anti-HIV, and anti-HCV.

Hepatitis B surface antibody was available in 299 (93.4%) students, and 278 (93.0%) of these were seropositive (Table 2). Median anti-HBs level was 263 mIU/mL (interval: 0-1000) [Interquartile range (IQR):55–785].

If the total group is divided into two subgroups, one of which had hepatitis B vaccine at birth (the cases born in and after 1998), and the other had not (the cases born in 1997); the difference in anti-HBs negativity prevalence is not significant between these two sub-groups (p=0.220). Median anti-HBs level was detected as 230 mIU/mL (0-1000) (IQR:76-735) in those born in the year 1997, and 276 mIU/mL (0-1000) (IQR: 51-790) in those born in and after the year 1998 (p=0.733).

Anti-HAV IgG was tested in 206 (64.4%) students; 35 (17.0%) of these were seropositive, 171 (83.0%) were seronegative. No relation was detected between age and anti-HAV IgG positivity (p=0.187).

Two doses of hepatitis A vaccine had been applied to 14 students before the study. Anti-HAV IgG was positive in five studens (35.7%). Anti-HAV IgG was positive in thirty (15.6%) of the students who had not received hepatitis A vaccine (p=0.067).

191 (59.7%) students were searched for anti-measles IgG and antimumps IgG. Anti-measles IgG was positive in 157 (82.2%), and anti-mumps IgG was positive in 179 (93.7%). There was no relation between age and seroprevalence of anti-measles (p=0.258) and anti-mumps IgG (p=0.920).

Anti-rubella IgG was studied in 207 (64.7%) students. It was positive in 204 (98.6%). There was no relation between age and anti-rubella IgG seroprevalence (p=0.960). All anti-rubella IgG seronegative students (n=3) were girls and 17 years old.

172 students were searched for anti-varicella zoster virus IgG. It was seropositive in 160 (93.0%). There was no relation between age and anti-varicella zoster IgG seroprevalence (p=0.922).

There was no relation between gender, income levels of the families, the education levels of the parents, smoking status and hepatitis A, hepatitis B, measles, rubella, mumps, varicella zoster seroprevalence (p>0.05).

21 NS who have a chronic disease, 17 were examined in terms of anti-HBs and anti-HBs of which two were negative. Anti-HBs was negative in nineteen (6.7%) of other 299 NS, who do not have chronic disease (p=0.339). No difference was also detected between the existence of a chronic disease and seroprevalence of hepatitis A, measles, rubella, mumps and varicella (p>0.05).

No difference was detected between prematurely born or term born students with hepatitis A, hepatitis B, measles, rubella, mumps, and varicella seroprevalence (p>0.05).

No difference was detected between obese/non-obese students and according to the weight percentiles (38 were under three percentile, 282 were equal or above three percentile) with hepatitis A, hepatitis B, measles, rubella, mumps, and varicella seroprevalence (p>0.05).

All the seronegative adolescent NS for any of the vaccine preventable infections tested in this study were referred for vaccination.

DISCUSSION

Our study showed that Turkish adolescent NS are under the risk of hepatitis A and measles. The ages of NS were 16-18 years in this study. No study in English literature about NS being in contact with patients and hospital environment at such a young age was found. In Turkey, there is a need for studies carried out among the NS on this subject in different regions of our country, like Çetinkol and Yıldırım study, which was conducted in Ordu province.[9]

Documentation of the immunization status at the time of registration to HCWs is recommended.[1,2,8] The HCWs and healthcare school students are in danger of being exposed to various infection factors during their hospital practice. If they have inadequate vaccination for vaccine-preventable diseases, besides their health being in danger, they may become a source of contamination for their classmates and of nosocomial infection in the hospital environment.[3-7] Because of this fact, seronegative The HCWs and healthcare school students for the vaccine-preventable diseases should be determined during registration and the appropriate vaccines must be applied.[1,2,8]

Among these vaccine preventable viral infections, hepatitis B virus is the most common virus transmitted among health personnel. About 40% of cases of hepatitis B and C in the healthcare industry around the world are caused by occupational exposure. The most infections caused by occupational exposure occur at the time of using needles that may contain blood.[13]

Turkey is a medium endemic country for hepatitis B virus transmission. Hepatitis B vaccine is applied routinely to babies and to the people in specific risk groups since 1998. In our study, anti-HBsAg level was detected ≥10 mIU/mL in 93.0% of the NS. Anti-HBsAg level was detected ≥10 mIU/mL in 89.0% of NS in the study carried out by Çetinkol and Yıldırım in the NS who were in the same cohort with our study for hepatitis B vaccine.[9] In two other studies conducted in our country, anti-HBs seropositivity was detected 65.8% and 87.0% in adolescents who were in the same age group and same vaccine cohort with our study group.[14,15] Higher anti-HBs seropositivity levels in these studies compared to the ones before introduction of hepatitis B vaccination in Turkey was attributed to introduction of a "National Hepatitis B Vaccination Program" beginning at birth, as well as catch-up vaccination with an “Extended Vaccination Programme” conducted in primary schools.

In our study, no seropositivity difference was found between the NS who had got three doses hepatitis B vaccine in infancy (the cases born in and after 1998) and NS who had not got hepatitis B vaccine in infancy (the cases born in 1997). This can be interpreted as the result of the implementation of the vaccination program to all NS in our study group during their primary education. There is a need for another research that would provide the data of hepatitis B seroprevalence in adolescents who were born in or after the year 2000; these children got three doses hepatitis B vaccines only in infancy and they were not vaccinated thereafter.

Table 2. Seroprevalence of antibodies against vaccine preventable diseases in nursing students

Antibody Test Results	n (%)*
Anti-HBs (n=299)**	
Positive	278 (93.0)
Negative	21 (7.0)
Anti-HAV IgG (n=206)**	
Positive	35 (17.0)
Negative	171 (83.0)
Anti-measles IgG (n=191)**	
Positive	157 (82.2)
Negative	34 (17.8)
Anti-rubella IgG (n=207)**	
Positive	204 (98.6)
Negative	3 (1.4)
Anti-mumps IgG (n=191)**	
Positive	179 (93.7)
Negative	12 (6.3)
Anti-varicella IgG (n=172)**	
Positive	160 (93.0)
Negative	12 (7.0)

*: Column percent, **: "n" shows the number of students this test was analyzed.
Anti-HBs: Hepatitis B surface antibody, **Anti-HAV IgG:** Hepatitis A antibody IgG

Hepatitis A is the most common cause of acute viral hepatitis in Turkey and other countries in the world. The infection is mainly observed during early childhood in the countries, which have high endemic, however in the countries which have good economical and hygienic measures, it is observed more frequently in adolescents and adults. Hepatitis A infection has good prognosis in childhood, but it may be fulminant and even mortal in adulthood.[16] Hepatitis A seroprevalence in adolescents in different regions of Turkey was detected as 52.4% in 14-18 years old group in İzmir province, 49.0% in 15-17 years old group in Konya, 47.3% in 14-16.5 years old group in Adana province, and 69.0% in 15-19 years old group in Istanbul.[17-20] A study conducted during the same years in Van province, however, determined a high seropositivity in 16-18 years old group, as 92.3%.[21]

The only study conducted in Turkey in the NS determined hepatitis A seropositivity as 39.5%.[9] Hepatitis A seropositivity in our study was 17.0%, which is lower than reported levels in the previous studies. This result suggests that hepatitis A sensitivity might be very high among the young adults in Ankara.

Hepatitis A vaccination in Turkey was routinely started in two doses in 18 and 24 months old children, soon in the year 2012. As stated above, in recent studies conducted in different regions of Turkey, there has been a tendency of decrease in hepatitis A seroprevalence rates.[17-20] Accordingly, because of high seronegativity rates and because of their being in the risk group of serious disease, it is suggested to consider vaccination of all Turkish adolescents against hepatitis A with a national campaign, even if they are not NS.

Measles vaccine is being applied since 1970 in Turkey. While it was just in the form of measles in previous years, it has been administered in the form of MMR in the "National Vaccine Schedule" since 2006.[11,12]

Compared to the general population, HCWs are estimated to be at 13- to 19-fold greater risk of acquiring measles.[22,23] Measles seropositivity in two different regions of Turkey was detected as 91.6% in female medical faculty students with mean age 20.5 years and 82.8% in nursing university students aged between 17-24 years.[24,25]

Measles seropositivity was 82.0% in our study group. No other research was conducted in Turkey investigating measles seroprevalence in adolescents in a similar cohort like our study group. There is a need for seroprevalence studies in Turkey, in child and adolescent age groups, to decide on the requirement of re-immunization or booster doses of measles vaccine.

It is known that ≥ 95% seropositivity is achieved with two doses of measles vaccines (provided that the first dose is after the 12th month).[16] In Turkey, in the year 2002, MMR vaccination rate was relatively low and reported as 82%, near that year the NS in our study group had a dose of MMR vaccine.[26] Our study group received four doses of measles vaccines; the first dose was received in the 9th month. Nevertheless, the seropositivity is low. We believe that the probable cause of this observation is low vaccination rate. Two doses MMR vaccination rate reached to 97% in 2009; it can be predicted that the seropositivity will be higher in the children who were vaccinated in this period, but there is a need for more studies about this subject.

In Japan, the single dose routine childhood measles vaccination schedule has increased to two doses in 2006. In 2008, they made a five years period catch up campaign for the measles-rubella vaccination to 13-18 age years old group. Measles specific immunoglobulin G was searched in the Japanese NS in 2007-2012 period; while the measles specific antibodies were detected as 52.7% in 2007, the value has risen to 96.6% after the campaign in 2012.[27]

92-95% vaccination coverage is required to achieve herd immunity and protect unvaccinated, susceptible individuals against measles. Suboptimal vaccination rates can lead to regular outbreaks.[28] There is an unimmunized or partially immunized group in Turkey because of the immense migration to Turkey. Considering the fact that the number of measles cases has increased considerably in the recent years; the result of our study indicates that a catch up campaign must be done in Turkey, like the one in Japan, in order to decrease public health risks, prevent the possible epidemics and eliminate the measles.[24]

Studies in two different regions of Turkey reported rubella seropositivity as 97.2% and 98.3%, mumps seropositivity as 93.5% and 83.3% in the medical faculty (mean age 20.5 years) and nursing university students (aged between 17-24 years), respectively.[24,25] In our study, rubella and mumps seropositivity were 98.6% and 93.7%, respectively in the adolescent NS, a similar result compared to other studies.

Since, routine vaccination for varicella zoster virus for one year old children have been initiated

after the year 2013, the adolescents in our study group did not have varicella vaccination (except a single person), and the varicella seropositivity was detected as 93.0%. The seroprevalence of varicella in children aged 7-15 was detected as 61.6% in Manisa province.[29] Another study done in İzmir province reported this rate as 81.2% in adolescents.[30] Varicella seroprevalence, which is the result of chickenpox disease undergone by a natural route, is high, similar to our study. Similar to hepatitis A, the risk of complications increases in the varicella infection during the adult period. Therefore, we suggest the varicella vaccination of the seronegative NS.

Examining the seroprevalence of hepatitis A, hepatitis B, measles, mumps, rubella and varicella and immunizing susceptible nursing students (NS) prior to contact with patients will prevent the adolescents from these contagious diseases during their health education and practice, as well as being a source of nosocomial infection. Adequate immunization and contact precautions are the primary ways to decrease this risk.

This study has some limitations. First, the study group relied on self-reported vaccination status. Second, there was not a control group.

CONCLUSION

This study examines the seroprevalence of vaccine-preventable infections in NS, a population with a high risk of exposure to the infectious agents than the normal population. The majority of NS were susceptible to hepatitis A virus (83.0%). We think that measles virus seropositivity was low (82.2%) in the study group. It is recommended that a 92-95% vaccination coverage is required to achieve herd immunity and protect unvaccinated, susceptible individuals against measles. We suggest pre-admission screening of the NS for the vaccine preventable diseases. Students with inadequate protection should be immunized prior to contact with patients.

Our study results might help to provide a scientific evidence for implementation of an immunization guideline and develop a policy to increase awareness about infections at admission to nursing schools.

The study also determined the immunization status of 16-18 years old healthy Turkish adolescents. Our study result suggests that there is a need to develop a strategy to increase the hepatitis A vaccination rate among adolescents. An additional dose of measles vaccine should be considered to this age group, also.

Appendix:

Your age....., Weight.....
Height:.....

Do you have a history of premature birth?
❒Yes ❒ No

Education level of your mother
- ❒ Illiterate
- ❒ Literate
- ❒ Primary school
- ❒ Secondary school
- ❒ High school/ University graduate

Education level of your father
- ❒ Illiterate
- ❒ Literate
- ❒ Primary school
- ❒ Secondary school
- ❒ High school/ University graduate

Income status of your family,
- ❒ Under the minimum wage
- ❒ Gets minimum wage
- ❒ Income is more than minimum wage

Smoking
- ❒ None
- ❒ Father
- ❒ Mother

I have the chronic disease .....
Do you have a vaccination card ?
❒Yes ❒ No

Did you have appropriate vaccines for the Ministry of Health Vaccination Schedule?
❒Yes ❒ No

Did you have an additional vaccine which is not in the Ministry of Health Vaccination Schedule?
❒Yes ❒ No

If yes, name of the vaccine ....., date of vaccination.....
Name of the last vaccine that you had....., date of vaccination.....
Did you ever use blood, blood product or steroid for any reason?
❒Yes ❒ No

If yes, when ?.....

*The authors declare that there are no conflicts of interest.

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